

B1
CONT.

The term "protein", when used herein refers to a chain of amino acids whose α carbons are linked through peptide bonds. Proteins include native proteins *in vivo* or isolated native proteins. Proteins also include chemically or recombinantly synthesized proteins. In addition, it is to be understood that the term proteins, as used herein includes the protein product as translated from an mRNA molecule as well as the protein products as subsequently modified. Thus proteins also include modified proteins such as glycoproteins, lipoproteins and the like.

Delete the paragraph at page 7, lines 19-29 and insert the following:

B2

--The terms "expression" or "release" of a protein when used herein in reference to a protein whose expression or release is altered under hypoxic conditions are used to indicate that alterations in detectable protein level are due to alterations in the physiological activity of the cell or tissue and not to attribute a particular mechanism to the observed alteration in detectable protein level. Thus the phrases in "increase in expression" or "increase in release" of a protein are used to indicate that some action of the subject cell or tissue results in an increase in the detected levels of that protein, either released to the environment (e.g., culture medium) or detected in a lysate. The increase can be due, for example, to increased expression of a gene encoding that protein, to defective expression of a native protein resulting in the detected protein "fragment", changes in uptake of the protein, changes in active secretion of the protein or changes in net release of the protein.--

9-22
Delete the paragraph at page 10, lines ~~4-16~~, and insert the following:

B3

--As used herein, the term "trophoblasts" includes the cytotrophoblast stem cells and lineages derived from these stem cells. The various lineages derived from cytotrophoblast stem cells are generally known to those of skill in the art. In humans, for example, two differentiation pathways exist for cytotrophoblasts, giving rise to populations that are morphologically and functionally distinct (Cross *et al. Science*, 266: 1508-1518 (1994)). In the first trimester, cytotrophoblast stem cells reside in chorionic villi of two types; "floating" villi that do not contact the uterine wall and "anchoring" villi that do contact the uterine wall. Cytotrophoblasts in the floating villi exist only as polarized epithelial monolayers, anchored to a basement membrane and surrounding a stromal core containing fetal blood vessels. These cytotrophoblasts, which are highly proliferative in the first trimester of gestation, differentiate exclusively by fusing to form a syncytial layer that covers the villus. Floating villi, which

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make up the fetal compartment of the placenta, are bathed by maternal blood and perform gas and nutrient exchange functions.--

Delete the paragraphs at page 10, line 27 through page 11, line 9, and insert the following:

B4
--A large body of evidence indicates that preeclampsia, and other diseases of pregnancy, are associated with highly characteristic abnormalities in placental development (referred to herein as an "abnormal maternal-placental interface") such that the placenta is only superficially connected to the uterus. Cytotrophoblast invasion is shallow and does not proceed beyond the decidual portions of the spiral arteries. (Redman, New Engl. J. Med. 323: 478 (1990); Brosens et al. Obstet. Gynecol. Annu. 1: 177 (1972) Gerretsen et al., Brit. J. Obstet. Gynecol., 88: 876 (1981); Moodley and Ramsaroop, S. Afr. Med. J., 75: 376 (1989)). In addition, not as many vessels show evidence of trophoblast invasion (Khong et al. Br. J. Obstet. Gynecol., 93: 1049 (1986)).

These morphological differences are a dramatic contrast to normal development (placental differentiation) in which, as explained above, the trophoblasts, detach from their basement membranes, aggregate, and invade much of the uterus and its arterial system thereby forming an intimate connection (the maternal-placental interface) between the mother and the fetus. As used herein, the term "abnormal placental function" refers to the physiological consequences of this abnormal placental development.--

In accordance with 37 CFR §1.121 a marked up version of the above-amended paragraph(s) illustrating the changes introduced by the forgoing amendment(s) are provided in Appendix A.

In the Claims:

Please amend the claims by substituting the following claims for the corresponding previously pending claims of the same number(s):

- B5
2. A protein of claim 1, wherein the protein is selected from the group consisting of:
- (a) Protein A having a molecular weight of about 21 kDa and a pI of 6.0 wherein the release of said protein, under hypoxic conditions, is increased;
 - (b) Protein B having a molecular weight of about 22 kDa and a pI of 7.0 wherein the release of said protein, under hypoxic conditions, is increased;